

REMARKS

Claim 91 has been amended to correct a typographical error. No other amendments are proposed with respect to the claims at this time.

Amendment was made to the specification to include continuation data in the Preliminary Amendment filed 15 July 2003.

Applicants appreciate the acknowledgement of the receipt of the amendment dated 10 January 2005; however, this amendment included claims 87-93 which have not been acknowledged.

Applicants also appreciate the withdrawal of the rejection for double-patenting.

All claims were rejected as assertedly anticipated by any of three Lanza patents, U.S. 5,690,907; 5,780,010 or 5,958,371. All of these patents are related as parent and continuations-in-part.

The Examiner is correct that these patents allude to the inclusion of therapeutic agents or drugs in compositions of nanoparticles similar to those that are the subject of the present claims. In the previous response, applicants argued that there is no disclosure in the cited Lanza patents that the claim requirement that the drug be contained in a lipid/surfactant layer that surrounds a fluorocarbon core in said particles. Rather, the location of the therapeutic agent is not disclosed.

As the Office is well aware, in order for anticipation to be found, each and every limitation of the claim must be found explicitly or inherently in a single prior art document. Clearly the limitation that the drug be contained in the lipid/surfactant layer is not explicitly disclosed in the Lanza patents, and it is not inherently disclosed either since no mode of preparation is found and the particles are hydrophobic throughout.

The Office considers that the drug would be expected to be contained in the lipid/surfactant layer provided the drug is hydrophobic, as is the case for many drugs that are the subject of the present invention. However, in support of its position, the Office states that “it is known in the art that the lipophilic agents get incorporated in the lipid bilayer of the liposomes and the hydrophilic agents in the interior.” The flaw in this argument is that the present compositions are not liposomes and there is no aqueous interior. Rather, the interior of the particles in the present application is hydrophobic as well as is the lipid/surfactant outer layer. There is no lipid bilayer associated with these particles and the rejection of applicants’ argument appears to be based on the misconception that the present invention concerns liposomes. As this is not the case, it is believed that applicants’ arguments must stand, and the prior art cited does not inherently disclose that the drug is contained in the lipid/surfactant layer. It will also be noted that there is no description in the cited Lanza patents of the mode of preparation of particles containing therapeutic agents, so the location of the therapeutic agent cannot be deduced from the mode of preparation either.

Thus, it is believed that the rejection of claims 71-79 and 82-86 for anticipation may be withdrawn.

Similarly, all claims were rejected as obvious over the three Lanza patents either alone or in combination with Adler-Moore (U.S. 5,656,287). Applicants agree with the assessment made by the Examiner of the teachings of Adler-Moore which is said to disclose a liposomal preparation of cyclosporin and teaches that water soluble molecules are incorporated into the aqueous interior and lipophilic molecules incorporated into the lipid layer. However, the present application is not concerned with the preparation of liposomes, and no similarity with regard to the preparation of the

present nanoparticles in Example 1 and the preparations of liposomes that would result in similar compositions is seen.

In Example 1 of the present application, doxorubicin is suspended in methanol and added to the surfactant layer where the surfactant layer is evaporated and dispersed into water by sonication, but then the suspension is transferred to a blender with perfluorooctylbromide and distilled. In this process of preparation, nanoparticles are formed containing a perfluorooctylbromide core coated with the lipid/surfactant layer and water is on the outside to form the emulsion. No liposomes result. In contrast, there is no addition of a hydrophobic core in the preparation process of Adler-Moore, and liposomes do result.

For the reasons stated above, applicants' argument has not been shown to be false. The secondary document cited by the Office concerns liposomal preparations. The claimed preparations are not liposomal, but themselves contain hydrophobic cores. The primary documents concern nanoparticles, but there is no description of the preparation of these particles to demonstrate that the therapeutic agents, even if hydrophobic, would be concentrated in the outer layer rather than distributed throughout the particles or concentrated in the hydrophobic core. Accordingly, this basis for rejection may also be withdrawn.

Applicants appreciate the withdrawal of the rejection of the claims over the combination of WO 95/03829 with Long.

Applicants await action on the remaining claims, claims 87-93. However, as these claims are dependent from claim 71, which is shown to be free of the art, it is believed that these remaining pending claims are free of the art as well.

Conclusion

The only substantive rejection of the claims is made over the art. The basis for the rejection appears to reside in the misapplication of art regarding liposomes to the present claims which concern perfluorocarbon particles coated with lipid/surfactant layers. There is no evidence of record to indicate that the primary documents describe processes which will result in the therapeutic agents being contained in the lipid/surfactant layer. This claim limitation is neither explicitly nor inherently disclosed in the primary documents. Accordingly, it is believed that all claims, claims 71-79 and 82-93, are free of the cited art and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 532512000401.

Respectfully submitted,

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By: Kate H. Murashige
Kate H. Murashige
Registration No. 29,959
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5112
Facsimile: (858) 720-5125